Thrombotic side-effects of lower limb venography

The use of heparin-saline flush

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Summary

In a prospective study of 256 postoperative patients, bilateral lower limb venography was performed using meglumine iothalamate followed by heparin-saline flushing of the deep veins, and the complications of the procedure were assessed. No patient developed clinical evidence of deep-vein thrombosis after the venogram. In 117 patients fibrinogen uptake was performed 24 hours after the venogram. A new positive area on the uptake scan developed in 3 patients (2,6%).

Local swelling or haematoma at the injection site occurred in 15 patients (5,9%), cellulitis in 2 (0,8%) and minor contrast reactions in 6 (2,3%). There were no major reactions and no procedure-related mortality.

The reasons for the wide variation in the reported incidence of post-venogram thrombosis are considered and the importance of heparin-saline flushing of the deep veins to prevent this complication is discussed.

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The symptoms and signs of lower limb deep-vein thrombosis (DVT) are notoriously nonspecific.[1,2] An incorrect clinical diagnosis, will result in inappropriate therapy with the attendant risk and cost of unnecessary anticoagulation. A clinically suspected DVT should be confirmed with an objective investigation.

Venography has a high sensitivity and specificity in the diagnosis of DVT and represents the reference standard against which other tests are compared. However, the perceived complications of venography, particularly venogram-induced DVT, have militated against its use.[3] The alternative non-invasive tests, which include Doppler ultrasound, impedance plethysmography and the ^{125}I fibrinogen uptake test, are less accurate than venography. If post-venogram complications could be reduced to acceptable levels the accuracy of venography would outweigh its disadvantages.

Patients and methods

During the period 1975-1984, 256 patients aged over 40 years, who compromised the control limb of a randomised study, underwent bilateral lower limb venography after major abdominal surgery. The design of the study allowed for critical evaluation of the methods and complications of venography.[4] None of these patients had received anticoagulants before the venogram.

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On the day before surgery, 100 μCi ^{125}I-labelled fibrinogen (Amersham, England) was injected intravenously, after thyroid blockade with sodium iodide. The count rate at fixed points on the legs was recorded pre-operatively and at daily intervals postoperatively using a portable ratemeter. A 20% rise in count, persistent for 48 hours or more, was regarded as a positive result.[5] If the central count levels dropped, ^{125}I fibrinogen was re-injected.

On the 6th postoperative day, bilateral ascending venography was performed using meglumine iothalamate (Conray 280). Fibrinogen uptake counts were done on 2 or more days after the venogram in 117 patients.

The method of venography was adapted from that described by Rabinov and Paulin.[6] The patient was placed in a semi-erect position with the contralateral foot weight-bearing, allowing the leg being examined to hang free. A 21-gauge butterfly needle was introduced into a suitable vein on the dorsum of the foot, a small amount of heparinised saline injected to establish patency and ensure against extravasation, and then the contrast medium injected under fluoroscopic control. Serial spot films were taken as far as the iliac veins, applying gentle calf pressure to move the contrast up the veins. The final exposures of the iliac veins and the inferior vena cava were taken after moving the screening table to the horizontal position. Usually 8 - 10 exposures were needed for the examination and 75 - 100 ml contrast material per limb was injected.

A tourniquet was not used during the examination. During the injection of contrast medium a light was kept focused on the injection site, observing for signs of extravasation. At the end of the examination 1 000 IU heparin diluted in 50 ml saline was injected to flush the contrast material from the deep veins.

The diagnosis of DVT was based on the presence of filling defects, abrupt termination of contrast-filled veins or non-filling of all or part of the deep system with collateral flow. The normal anatomy of the deep veins and the diagnostic pitfalls have been well described by Lea Thomas.[7]

Results

Venography demonstrated DVT in 20,8% of patients. In approximately half the cases it was bilateral and in most it was restricted to the calf.

Swelling or bruising at the injection site was noted in 15 patients (5,9%). In most cases this was asymptomatic, but a few patients complained of local pain. Cellulitis developed in 2 patients (0,8%) and minor contrast reactions, including dizziness, vomiting, urticaria, peri-orbital swelling and bronchospasm, occurred in 6 (2,3%). There were no major reactions and no procedure-related deaths.

In 3 patients venography was performed on one side only. Two of these patients vomited after the injection into the first limb and in one no suitable vein was found. None of the patients had clinical evidence of DVT after the venogram. Radio-active fibrinogen uptake studies were continued for at least 24 hours after the venogram in 117 patients. Positive uptakes were recorded in 9 patients (9 legs). Six of these had already shown evidence of superficial or DVT on the veno-

gram. Thus 3 patients (3 legs) developed a new positive fibrinogen uptake scan after the venogram (2,6% of patients, 1,3% of legs).

Discussion

Controversy still exists with regard to venography with ionic contrast media, some writers being of the opinion that the thrombotic complications are sufficiently severe to warrant the routine use of non-ionic materials despite very high cost[8] or abandoning venography for the routine diagnosis of suspected DVT.[3]

Venous thrombosis as a complication of venography has been reported as occurring in up to 50% of patients.[9] Bettman and Paulin[10] observed that 32% of patients developed erythematous swelling of the lower limb 12 - 24 hours after negative venography using meglumine ditrizoate (Renografin).[10] They termed this a 'contrast-related inflammatory response' and postulated that it was due to contrast-related endothelial damage, and possibly even thrombophlebitis in some patients.

More recent series have attempted to define the prevalence of post-venographic DVT with the use of the ^{125}I fibrinogen uptake test. A number of studies using ionic contrast materials have recorded high uptakes in the lower leg, interpreted as representing DVT in 7 - 55% of patients.[8,9,11-13] The interpretation of these findings is far from straightforward. Factors that may influence the wide variation in reported incidence include the criteria of positivity for the fibrinogen uptake test, the underlying disorder dictating the need for venography, the venographic technique, the contrast material used and the concomitant use of anticoagulants. The ^{125}I fibrinogen test lacks specificity for the diagnosis of DVT. Local high uptakes may be demonstrated in any condition in which fibrin is deposited, such as superficial vein thrombosis, oedema, cellulitis and haematoma. It is tempting to speculate that transient contrast-induced damage to the venous wall or endothelium and not necessarily venous thrombosis may be the cause of a proportion of elevated fibrinogen counts. Most patients who develop a positive scan after venography do so in the first 48 -72 hours and the majority of high counts are concentrated in the ankle region.[11] Venography may therefore induce a chemical phlebitis or periphlebitis that may or may not be associated with thrombosis.

The only method currently available to elucidate the precise significance of a positive post-venogram scan is a repeat venogram. This is impractical and probably unethical. Albrechtson and Olsson[12] reported the development of a positive fibrinogen uptake in 20 of 61 patients who had an initially normal venogram. A second venogram was performed in 4 cases and fresh thrombus shown in 2. Ritchie *et al.*[11] reported development of a positive scan in 30 of 55 limbs (55%) after venography, with the majority of high counts restricted to the ankle region; 3 patients became symptomatic with raised counts above the level of the knee, and thrombosis was confirmed in 2 of them, who were submitted to repeat venography. The remaining 27 limbs remained asymptomatic.

Comparisons between ionic and non-ionic contrast materials with respect to contrast-related complications have been reported. Using the ^{125}I fibrinogen uptake test, Walters *et al.*[8] found a positive result in 28,6% of limbs after an ionic contrast material (Conray 280) and 3,6% of limbs after a non-ionic one (metrizamide). Similar results were reported by Lea Thomas *et al.*[13] with a 26,7% incidence after Conray 280 and 3,3% after Hexabrix.[13] The results in these studies were not confirmed venographically.

The low incidence of raised fibrinogen counts in our study may be due to the techniques employed. Firstly, a tourniquet was not used to direct the contrast medium to the deep veins, reducing the pressure as well as the contact time of the contrast with the vessel wall, and secondly, after the procedure heparin in saline (1 000 IU 50 ml) was used to flush the deep veins with screening of the limbs to ensure that no residual contrast remained.

Little mention of the heparin saline flush has been made in the literature and it does not appear to be widely practised. The first study[14] mentioning its use was published in 1979 and noted that the incidence of clinically diagnosed post-venogram thrombophlebitis was reduced from 4,4% to 2% using 1 000 IU heparin in 250 ml 5% dextrose as an infusion into the limb. A second study[15] reported an incidence of post-venogram DVT of only 3,3% diagnosed on fibrinogen uptake after a flush of 10 000 IU heparin. In both these studies ionic contrast media were used. It should be noted, however, that neither of these two studies was randomised. Furthermore, the claimed reduction in thrombophlebitis after venography attributed to heparin saline flush by Arndt *et al.*[14] is not statistically significant when their data are recalculated ($P = 0,38$; chi-square test with Yates's correction). Heparin in high concentration may in fact injure venous endothelium close to the site of injection, as demonstrated in an animal model by Franz and his colleagues.[16]

Ideally our study should have been randomised to a saline versus a heparin saline completion flush. It is conceivable but unproven that the mere mechanical clearance of contrast is as beneficial as the addition of heparin. Our goal, however, was not specifically to examine the use of a heparin saline flush but to audit the morbidity of an established venographic technique in our institution. In this regard the incidence of complications we recorded compares favourably with the incidence in studies using non-ionic contrast materials. This would suggest that the cheaper ionic contrast materials can be used with acceptably low morbidity provided a careful technique is followed.

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